The length of time of drug administration varied from two to twelve days. Eighty-three per cent of the total number did not receive the drug longer than five days.

The time required for the temperature to reach normal varied. In 84 per cent of the cases normal temperature was reached in forty-eight hours; in 59 per cent of the total cases this occurred in the first twenty-four hours. Cases requiring longer than six days usually had some complication which the drug did not affect. It is interesting to note that 31 per cent (thirty-nine cases) had subnormal temperatures which persisted for several days.

The blood concentration of the drug was unpredictable. It varied from a trace to a high of 17.9 milligrams per cent. No explanation is offered for this variability. When the drug was given rectally we found the blood concentration to be about half that of the orally treated cases.

Complications of the drug and the disease are discussed at some length.

Mortality for the entire series is 0.8 per cent.

CONCLUSIONS

With the experiences gained in this study we feel justified in drawing the following conclusions:

1. Sulfapyridine is a very effective drug that should be used in every clearly defined pneumococcic pneumonia in children.
2. It is reasonable to expect that sulfapyridine or related compounds will replace all other methods of routine treatment in the pneumococcus pneumonias in pediatrics practice.
3. The routine use of sulfapyridine in clearly defined pneumococcic pneumonias in childhood should markedly reduce the present death rates in this disease.
4. Sulfapyridine is a toxic and dangerous drug especially affecting the blood, blood-forming organs and the kidneys. Every case in which the drug is used is fraught with potential difficulties which may come with alarming suddenness and severity.
5. The drug should never be used unless the patient is completely under the control of the physician who should resort to frequent blood counts and urinalyses.
6. The drug should not be continued over long periods.
7. The drug apparently does not hasten the time of complete resolution and may even slightly retard it.
8. When treated early with sulfapyridine, the lobar pneumonias do not seem to progress on to the massive consolidation so frequently seen in the untreated case.
9. Routine determination of blood concentration is not necessary since no definite level can be established.
10. The degree of blood concentration seemingly has little effect on the speed with which the drug acts or with its ultimate effectiveness.

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POLYPOID BRONCHIAL TUMORS*

WITH SPECIAL REFERENCE TO BRONCHIAL ADENOMATA

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POLYPOID bronchial tumors are those neoplasms which grow as projections within the bronchial lumen and are visible through the bronchoscope. Until a short time ago, all invasive polypoid bronchial tumors were believed to be malignant. Recently,[1,2] however, polypoid bronchial adenomata have been separated, clinically and pathologically, from the other polypoid tumors, to form a new clinical entity—a polypoid bronchial tumor which, though locally invasive, rarely metastasizes and can be cured.

TYPES OF POLYPOID TUMORS

Since bronchial adenomata are polypoid in form, though nonmetastasizing, and comprise some 6 per cent[3] of all bronchial tumors, it becomes important to classify polypoid tumors in order to select the proper therapy. Three types may be distinguished, namely:

Metastasizing polypoid tumors (carcinoma).

Locally invasive, but nonmetastasizing polypoid tumors (adenoma).

Noninvasive, nonmetastasizing, purely local polypoid tumors (fibroma, lipoma, myoma, and so forth).[4]

The importance of this reclassification, and the recent separation of adenomata from carcinomata, are demonstrated by a review of some of the publications which resulted from their confusion. It seems most probable that certain reports of the successful removal of carcinoma of the lung by means of the bronchoscope,[5-9] and of the cure of carcinoma of the lung by pneumonectomy,[10-13] or deep x-ray therapy,[14,15] actually refer to cases of adenoma.

The various names by which the clinical entity now termed "bronchial adenoma" has been designated have added still further to the confusion. Geipel,[16] in 1931, termed these tumors "basal-cell cancer"; Wessler[2] (1932), "benign bronchial adenoma"; Kernan[17] (1935), "carcinoid"; Moersch[8] (1935), "adenocarcinoma"; Clerf and Crawford[18] (1936), "benign glandular tumors"; Zamora and Schuster,[19] (1937), "vascular adenoma"; Welt and Weinstein,[20] (1937), "endothelioma"; and, finally, Womach and Graham[21] (1938), "mixed tumors of the lung." Yet, undoubtedly, each of these authors referred to the same type of tumor.

RELATION TO AGE AND SEX

The age of the patient at the onset of symptoms of adenoma is strikingly different from that of

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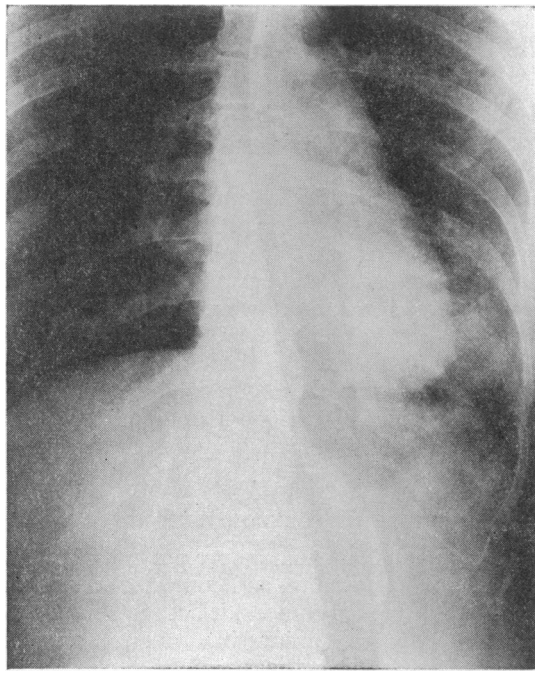

Fig. 1

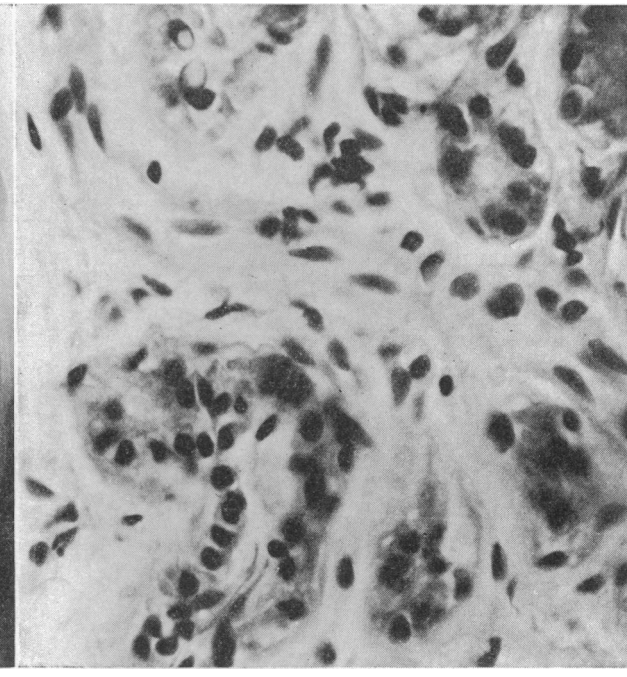

Fig. 2

Fig. 1 (Case 1).—Postero-anterior view showing the cystic whorls behind the left border of the heart. The barium in the esophagus shows no external pressure defects.

Fig. 2 (Case 1).—Photomicrograph (750 x) of the specimen removed at bronchoscopic biopsy from the endobronchial portion of the adenoma obstructing the mediastinal branch of the left lower lobe. Note the alveolar patterns and pyknotic nuclei. Compare with Fig. 3.

patients with carcinoma. In our group of eighteen patients with bronchial adenomata, twelve, or 66⅔ per cent, had symptoms before the age of forty years, in contrast to only 13 per cent of those with carcinoma, as shown in Fischer's[22] large series, and 11 per cent in Brunn's.[23]

The distribution by sex is likewise in marked contrast to that of carcinoma. In our eighteen cases of adenoma, ten, or 56 per cent, were females, whereas only 25 per cent of carcinomata occurred in females in Simpson's[24] and Gazagerli's[25] series.

In prognosis and duration of life, also, patients with adenoma present a marked contrast to those with carcinoma. If all cases of probable adenoma which have been reported as carcinoma are excluded, a few probable "five-year cures" of true bronchial carcinoma remain[26, 27, 11, 9, 28, 29]; the prognosis for patients with adenoma, on the other hand, is very good, and many "five-year cures" have been reported. In our series, for example, all the patients but one lived more than three years after the onset of the symptoms; fourteen lived more than five years. These figures are noteworthy since, in Brunn's[23] cases of carcinoma, only 4 per cent of 297 patients survived three years or longer.

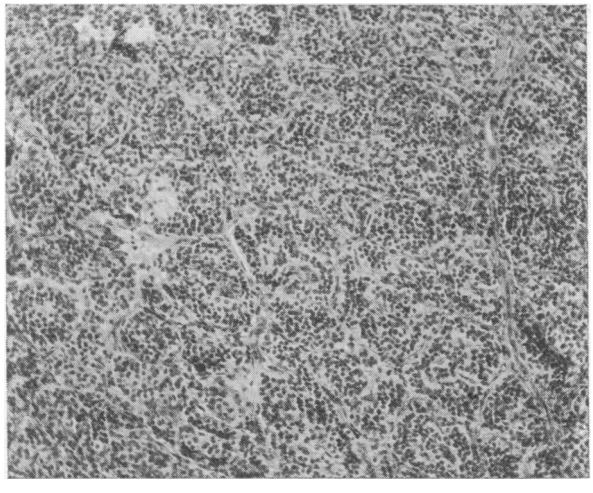

Fig. 3 (Case 1).—Photomicrograph (120 x) of a section of the extrabronchial portion of the tumor, showing the more definite alveolar pattern and its uniformity. No mitotic figures could be seen.

SYMPTOMS AND CLINICAL COURSE

The symptoms and clinical course of bronchial adenomata are related to three peculiarities of their life history: first, their location in a major bronchus; second, their slow growth; and, third, their vascularity.

Any lesion encroaching upon the lumen of a large bronchus gives rise to symptoms of bronchial obstruction, and the first symptoms of these tumors result from disturbance in the transference of air along the large bronchial tubes. Wheezing, "asthma," irritating, nonproductive cough, dyspnea, transient chest pains, "choked-up sensations" and respiratory postural discomfort are thus the initial symptoms to appear. These are often so indefinite or transient as to be entirely overlooked unless they are very carefully inquired for. When air becomes completely shut off from the alveoli distal to the tumor, atelectasis results, and this occurred in seventeen of our eighteen patients. On the other hand, when air is entrapped distal to the tumor, emphysema occurs.

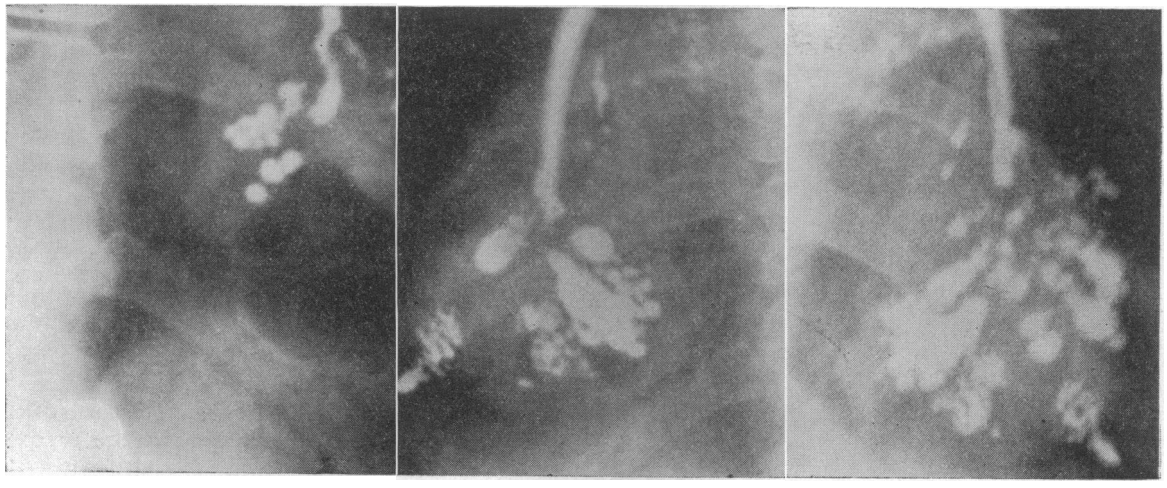

Fig. 4*a* Fig. 4*b* Fig. 4*c*

Figs. 4*a*, 4*b*, 4*c* (Case 1).—Serial selective "spot films" showing cystic dilatations in the mediastinal section of the left lower lobe.

As the tumor grows, the bronchial obstruction also interferes with the drainage of bronchial secretions; consequently, the next symptoms to appear are those of pulmonary suppuration. Recurring "pneumonias," or so-called drowned lung, are most common; but empyema, abscess and bronchiectasis are frequent. Twelve of our eighteen patients had marked symptoms of pulmonary suppuration, while the remaining six had only slight symptoms of suppuration, although bronchial obstruction was present. The obstructions in five of the latter, however, were in the upper lobe bronchi, and only one was in the lower lobe. When death occurs it usually is the result of the suppuration or an infection complicating the therapy.

The slow growth of these tumors allows time for permanent chronic inflammatory changes to occur in the lungs and pleura. Thus are produced chronic suppuration and toxemia, which give rise to easy fatigue, low-grade fever, chronic cough, sputum, pleuritic pains, dyspnea on slight exertion, anemia, anorexia, and all the symptoms usually associated with pulmonary tuberculosis. In six, or 33⅓ per cent of our patients, the erroneous diagnosis of pulmonary tuberculosis had previously been made.

The cardinal symptom of bronchial adenoma is the pulmonary hemorrhage associated with the extreme vascularity of these tumors. These hemorrhages are characteristically sudden in onset and termination, bright red in color, profuse even to the extent of producing shock, unprovoked by cough or exercise; and, in women, frequently occur during the menstrual period. This hemorrhage probably arises from the tumor itself. A second type of hemorrhage, associated with the distal suppuration, is just as frequent. It is composed of dark blood, often clotted and mixed with pus; is induced by cough and exertion, and is followed by blood-streaked sputum for several days. Pulmonary hemorrhage was a cardinal symptom in twelve, or 66⅔ per cent of our patients. This, however, has been reported as the immediate cause of death in only one case.[3] All the symptoms described are related to the endobronchial portion of the tumor; few symptoms or none are produced by the extrabronchial or mural portions.

Roentgenologically, the appearance is bizarre; but, characteristically, lobar atelectasis is present.[30] Disturbances in aeration characterize the picture, so that varying degrees of emphysema and atelectasis are present. A marked shift of the mediastinum, thick pleura, cystic whorls and abscess cavities represent the results of the suppuration. The tumor itself is rarely demonstrated, usually because of the inflammatory changes overlying it.

Bronchography, particularly with "endobronchial probing,"[31] is valuable in determining the level of the bronchial obstruction and the condition of the distal bronchi.[32] (Figs. 4*a*, 4*b*, 4*c*, 4*d*, Case 1.)

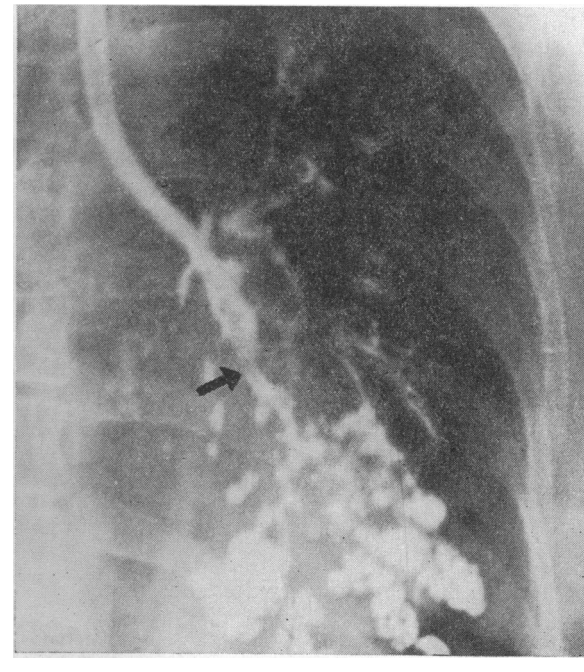

Fig. 4*d*.—"Spot film" showing the filling defect (arrow) at the site of the endobronchial portion of the tumor.

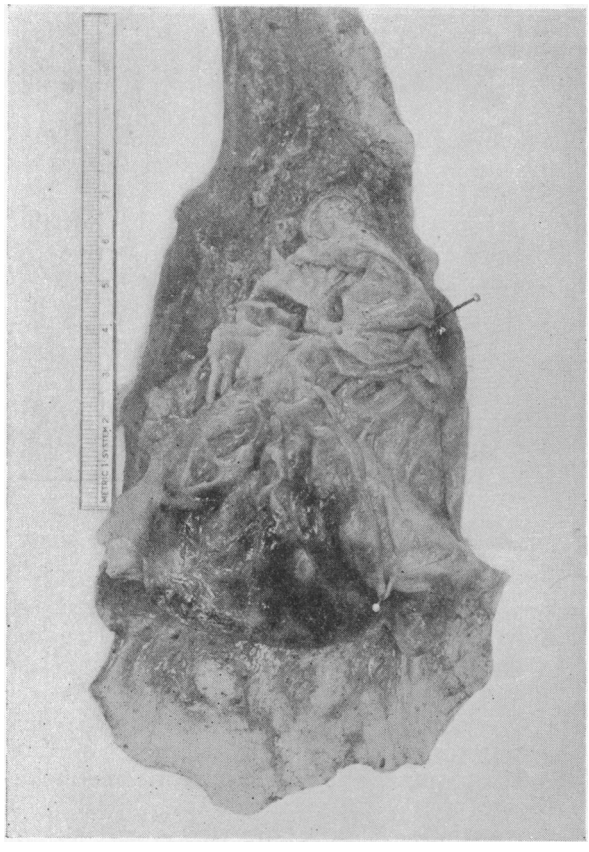

Fig. 5 (Case 1).—Specimen removed at lobectomy (left lower lobe), demonstrating cystic bronchiectasis limited to the mediastinal segment of the left lower lobe.

The bronchoscopic image is that of a soft or firm mass or polyp, whitish, pink or purple, not cystic, and, if of long duration, indurated and hard. These tumors are covered with mucosa and occasionally vessels traverse the bosselated surface. Their attachment to the bronchial wall is usually no more than a centimeter in diameter, and when this tumor is removed its stalk may be seen descending between the cartilaginous rings. The bronchus around the tumor is distended and its cartilages are thinned out or even absent.

DISTRIBUTION IN AUTHOR'S STUDY

In eleven (61 per cent) of our patients, the adenoma was on the left side, and in seven, or 39 per cent, on the right. Carcinoma, on the other hand, occurs slightly more often on the right side than on the left—53 per cent on the right in Fischer's[22] 3,435 cases; 57 per cent on the right in Brunn's[23] series. In our patients the lobes and bronchi were involved in the following order: left stem, 5; right stem, 4; left lower, 4; left upper, 2; right upper, 2; right lower, 1; and right middle, 0.

Three forms of adenoma were found in our group:

1. Endobronchial, usually with a small pedicle—five patients.
2. Intramural, usually with a broad pedicle—four patients.
3. Endo-extrabronchial, dumbell-shaped, with the extrabronchial portion usually the larger—nine patients.

HISTOLOGY

Histologically,[3,21] bronchial adenomata are characterized by a uniformity of cell type, absence of mitotic figures and a tendency for the cells to be grouped in an alveolar arrangement. Covering the tumor is the mucosa, which usually undergoes squamous-cell metaplasia and is separated from the epithelial portion of the tumor by a dense membrane of fibrous tissue. Beneath this membrane the epithelial surface is highly vascular.

Histological diagnosis of adenoma from the material removed at bronchoscopic biopsy is not easy, because the tissue obtained often is not deep enough within the tumor to show characteristic patterns. Squamous-cell carcinoma, because of the squamous-cell metaplasia present on the mucosal surface; angioma due to the vascularity just beneath the connective tissue capsule, or inflammatory tissue when the epithelial surface has been traumatized, may be diagnosed instead of adenoma.

TREATMENT

Treatment of the bronchial adenoma requires, first of all, the relief of toxemia by the reëstablishment of bronchial drainage.[33] This is accomplished by bronchoscopic removal of the endobronchial portion of the tumor. If disabling symptoms from the residual pulmonary suppuration persist in spite of postural drainage, lobectomy or pneumonectomy is required. It does not appear to us necessary for the maintenance of life to remove the tumor *in toto*. Residual mural portions of the tumor apparently remain quiescent for years. If, on repeated clinical, bronchoscopic and roentgen examinations, the residual mural or extrabronchial portions of the tumor show signs of an increased rate of growth, pulmonary resection is indicated. Deep x-ray therapy may offer some benefits, but we have seen no direct evidence that this form of therapy affects the tumor *per se*. Complicating suppurative disease, such as abscess or empyema, or both, may require surgical drainage.

Of the eighteen patients, thirteen are still living. Of these, two had pneumonectomy, one had lobectomy, four had bronchoscopic removal of the tumor, and six had deep x-ray therapy. Five patients died; one after pneumonectomy, one after bronchoscopic cauterization, and one after numerous bronchoscopic drainages (the tumor was not removed). The remaining two had no treatment; the diagnosis was made at necropsy.

The case reported below illustrates most of the salient features of the bronchial adenoma.

REPORT OF CASE

CASE 1.—F. J., a white female, 26 years of age, was admitted to the San Francisco Hospital (Tuberculosis Service of Dr. S. Shipman) on August 31, 1938. Her illness began in 1932 with wheezing and "asthma," followed by pulmonary hemorrhages, sudden in onset and termination, often occurring with the menses. During the next six years the hemorrhages were replaced by febrile periods terminating with the expectoration of bloody fetid sputum. The latter became more frequent until they were occurring every three weeks at the time of her admission to the hospital.

X-ray examination showed cystic whorls behind the left border of the heart (Fig. 1, Case 1); these shadows varied

in appearance from time to time. Repeated examinations of the sputum failed to reveal tubercle bacilli.

The clinical diagnosis was tuberculosis of the lungs. The patient had been treated by several physicians, and bronchoscopic and lipiodol examinations had been performed without demonstrating the pathological changes.

Bronchoscopy, done at the San Francisco Hospital in August, 1938, showed a small polypoid tumor obstructing the mediastinal branch of the left lower lobe (Fig. 4*d*, Case 1). Biopsy proved this tumor to be an adenoma (Fig. 2, Case 1). Endobronchial probing with serial selective bronchography[31] showed cystic bronchiectasis limited to the mediastinal segment of the left lower lobe (Fig 4*a*, 4*b*, 4*c*, 4*d*, Case 1).

A one-stage lobectomy (left lower lobe, Fig. 5, Case 1) was performed on October 10, 1938. The patient's convalescence was uncomplicated. The pedicle of the tumor left in the stump was not visible through the bronchoscope one month after operation. The extrabronchial portion of the adenoma which was removed showed the typical cellular pattern of an adenoma (Fig. 3, Case 1).

Eight months after operation the patient was free from symptoms, and bronchoscopy again showed no visible tumor.*

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CLINICAL NOTES AND CASE REPORTS

GASTRIC CARCINOMA: PITFALLS IN EARLY DIAGNOSIS*

By SAMUEL P. BURRE, M. D.
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WE all acknowledge without debate the distressing difficulties arising in the diagnosis of early carcinoma of the stomach. The importance of early recognition shall well be appreciated when we note that one-third of deaths from cancer in the United States originates in the stomach. Stereotyped, textbook description of gastric carcinoma with absence of free hydrochloric acid, enlarged lymph nodes, occult blood, or the presence of tumor tissue in stomach washings, are not infrequently premortem findings and beyond the stage of surgical redemption. Incipient cases, on the other hand, present symptoms that are notably

* Read before the staff of St. Joseph's Hospital, Eureka, January 18, 1940.